

Departement für Kleintiere, Klinik für Kleintiermedizin
der Vetsuisse-Fakultät Universität Zürich

Direktorin: Prof. Dr. Claudia Reusch Dipl. ECVIM-CA

Clinical characteristics and causes of pruritus in cats: a multicenter study on feline hypersensitivity-associated dermatoses

Inaugural-Dissertation

zur Erlangung der Doktorwürde der
Vetsuisse-Fakultät der Universität Zürich

vorgelegt von

Stefan Hobl

Tierarzt von
Walenstadt-Berschis SG

Genehmigt auf Antrag von

Prof. Dr. Claude Favrot, Referent

Prof. Dr. Michael Hässig, Korreferent

Zürich 2011

Table of contents

1.	Abstract	P. 1
2.	Introduction	P. 1-2
3.	Material and methods	P. 2
3.1.	<i>Study subjects</i>	<i>P. 2</i>
3.2.	<i>Study design</i>	<i>P. 2</i>
3.3.	<i>Establishment of tentative diagnoses</i>	<i>P. 2</i>
3.4.	<i>Statistical analyses</i>	<i>P. 2</i>
4.	Results	P. 2-6
4.1.	<i>Study population</i>	<i>P. 2</i>
4.2.	<i>Clinical features of cats with nonflea HD</i>	<i>P. 3</i>
4.3.	<i>Comparisons between cats with nonflea HD and those with flea HD</i>	<i>P. 3-5</i>
4.4.	<i>Comparisons between cats with food HD and those with nonflea/nonfood HD</i>	<i>P. 5</i>
4.5.	<i>Comparisons between cats with nonflea HD and those with other diseases</i>	<i>P. 5-6</i>
5.	Discussion	P. 6
6.	Acknowledgements Journal	P. 6
7.	References	P. 6-7
8.	Summary	P. 7-8

Clinical characteristics and causes of pruritus in cats: a multicentre study on feline hypersensitivity-associated dermatoses

Stefan Hobi*, Monika Linek†, Geneviève Marignac‡, Thierry Olivry§, Luc Beco¶, Claudia Nett**, Jacques Fontaine††, Petra Roosje‡‡, Kerstin Bergvall§§, Sveta Belova¶¶, Stefanie Koebrich***, Didier Pint†††, Marcel Kovalik‡‡‡, Sabrina Meury*, Sylvie Wilhelm*,¹ and Claude Favrot*,¹

*Dermatology Department, Clinic for Small Animal Internal Medicine, Vetsuisse Faculty, University of Zurich, Zurich, Switzerland

†Tierärztliche Spezialisten, Hamburg, Germany

‡Unité de Parasitologie, École Nationale Vétérinaire d'Alfort, Maisons-Alfort Cedex, France

§Department of Clinical Sciences and Center for Comparative Medicine and Translational Research, North Carolina State University, Raleigh, NC, USA

¶Clinique Vétérinaire, Spa, Belgium

**Dermatologie und Allergologie für Tieren, Kleintierklinik Rigiplatz, Cham, Switzerland

††Clinique Vétérinaire, Bruxelles, Belgium

‡‡Division of Clinical Dermatology, Department of Clinical Veterinary Medicine, Vetsuisse Faculty, University of Bern, Bern, Switzerland

§§Department Clinical Sciences, Swedish University of Agricultural Sciences, Uppsala, Sweden

¶¶Department of Therapy, Institute of Veterinary Medicine and Animal Science, Estonian University of Life Sciences, Tartu, Estonia

***Bruchweg 3, D-68809, Neulussheim, Germany

†††Unité de Dermatologie, VetAgro Sup Campus Vétérinaire, Marcy L'Etoile, France

‡‡‡The University of Edinburgh, Veterinary Dermatology Unit, Division of Veterinary Clinical Sciences, The Hospital for Small Animals, The Royal (Dick) School of Veterinary Studies, Edinburgh, UK
Correspondence: Claude Favrot, Dermatology Department, Clinic for Small Animal Internal Medicine, Vetsuisse Faculty, University of Zurich, Winterthurerstrasse 260, 8057 Zurich, Switzerland.
E-mail: cfavrot@vetclinics.uzh.ch

¹Both the authors contributed equally to this work.

Sources of Funding

Novartis Animal Health, Basel, Switzerland and research funds from the University of Zurich financed this study.

Conflict of Interest

No conflicts of interest have been declared.

Abstract

Hypersensitivity dermatitides (HD) are often suspected in cats. Cats with HD are reported to present with one or more of the following patterns: miliary dermatitis, eosinophilic dermatitis, self-induced symmetrical alopecia or head and/or neck excoriations. Previous reports on feline HD included small numbers of animals, took place in geographically restricted areas or did not compare these conditions with other causes of pruritus. The goal of the present study was

to analyse 72 parameters covering signalment, clinical, laboratory and treatment characteristics from a large group of pruritic cats from different geographical areas. Of the 502 cats, the following diagnoses were made: flea HD (29% of cases), food HD (12%) nonflea/nonfood HD (20%) and other diseases in which pruritus was a feature (24%). Cats with signs consistent with a HD but which did not complete a food trial were not analysed further (15% of cases). Most cats with nonflea HD exhibited signs compatible with one or more of the four typical lesional patterns, but none of these patterns was found to be pathognomonic for any specific diagnosis. Food HD and nonflea/nonfood HD were found to be clinically undistinguishable. Young adult, purebred and female cats appeared predisposed to nonflea/nonfood HD. As many diagnoses presented with similar lesional patterns, a thorough clinical work-up is required for establishment of a specific diagnosis.

Accepted 13 January 2011

Introduction

Hypersensitivity dermatitides (HD) are often suspected in companion animals, and these include flea bite hypersensitivity dermatitis, cutaneous adverse food reactions, urticaria, angioedema and atopic dermatitis (AD).¹ The use of the term 'feline AD' remains debatable, however, because its clinical presentation and histological features differ markedly from those of its human and canine counterparts. Furthermore, the use of the adjective 'atopic' (meaning 'IgE-mediated') itself is questionable for this disease, because the importance of IgE in its pathogenesis has not been firmly demonstrated.^{2,3} Very few studies have investigated the role of IgE in the development of HD in cats.^{2,4-6} Additionally, there is evidence suggesting the heterogeneity of feline IgE and that allergen-specific IgE serum levels do not correlate with clinical signs of HD in cats.⁷⁻⁹ Finally, one study reported that up to 35% of cats with HD have negative allergen-specific intradermal and serological tests.² Therefore, and following the current nomenclature of human and canine allergic skin diseases,^{10,11} as long as the importance of IgE has not been firmly demonstrated in cats with pruritic allergic skin diseases, the authors of this paper will not use the term 'feline AD' and replace it with the more generic term of 'HD'.

The diagnosis of feline nonflea HD (i.e. nonflea bite-associated HD) is usually based on the exclusion of

other pruritic diseases, such as ectoparasites (i.e. fleas, *Otodectes cynotis*, *Notoedres cati*, *Demodex gatoi*, *Neotrombicula* species), fungal infections (dermatophytes, *Malassezia* species) and bacterial infections. Additionally, other conditions must be ruled out depending on the clinical pattern (e.g. psychogenic alopecia for symmetrical self-induced alopecia, viral diseases for head and neck excoriations, and mast cell hyperplasia or tumours for eosinophilic dermatitis). Cats with nonseasonal HD should undergo a 6–8 week restriction diet to determine the importance of food allergens in the development of the condition and to identify cases in which food ingredients are the cause of flares. Although results should be interpreted cautiously, allergen-specific intradermal and/or IgE serological testing can be helpful to identify environmental allergens associated with hypersensitivity.

It is anticipated that cats with nonflea HD will exhibit pruritus and at least one of the following patterns: head and/or neck excoriations, usually symmetrical self-induced alopecia, eosinophilic diseases (eosinophilic plaques or granulomas, indolent ulcers) or miliary dermatitis. Some authors also reported other presentations, such as pododermatitis, facial erythema, seborrhoeic disorders or ceruminous otitis.^{1,2,12,13} To date, none of the signs or patterns reported above is considered pathognomonic for nonflea HD in cats.

To the authors' knowledge, reports of cats with HD have been scarce and have involved small numbers of affected cats. The main objectives of this multicentre study were to describe a large population of pruritic cats and to compare several populations, as follows: pruritic cats with flea HD, nonflea HD, food HD and those with other skin diseases in which pruritus was a feature.

Materials and methods

Study subjects

Pruritic cats were included by several veterinary dermatologists from different geographical areas of the following nine countries: Belgium (L.B., Spa; J.F., Bruxelles), Estonia (S.B., Tallin), France (Didier Noel Carloti, Bordeaux; G.M., Paris; D.P., Lyon), Germany (S.K., Neulussheim; M.L., Hamburg; Nina Thom, Giessen), Greece (Manolis Saridomichelakis, Thessaloniki), Sweden (K.B., Upsalla and Stockholm), Switzerland (C.F. and S.W., Zurich; C.N., Hüneberg; P.R. and Silvia Ruefenacht, Berne), UK (Paul Coward, London; M.K., Edinburgh) and USA (T.O., Raleigh, NC, USA).

Study design

Cats were included if they presented with chronic pruritus (at least two episodes or more than 2 months duration) and a definitive diagnosis had been made. Most cats were enrolled prospectively ($n = 390$), but some ($n = 198$) were also included retrospectively with the caveat that the owner-assessed pruritus score and some environmental information (e.g. lifestyle) might be missing [Corrections to data added on 1st April 2011 after online publication: '($n = 196$)' was changed to '($n = 198$)']. All data were collected and analysed at the University of Zurich by three of the authors (S.H., C.F. and S.W.); records were reviewed for verification of satisfaction of enrolment criteria.

At the time of inclusion, investigators recorded signalment and history and 72 parameters that included the age at pruritus onset, way of life, food, pruritus intensity, skin lesions and their distribution, the presence of concurrent clinical signs, outcomes of previous treatments, results of previously performed tests (e.g. blood panels), treatment outcome and final diagnosis. The minimal work-up needed

for inclusion of cases in this study was an adequate flea control, skin scrapes and a fungal culture. Skin cytologies were carried out whenever deemed necessary.

Establishment of tentative diagnoses

Diagnoses had to be based on at least one positive result of one specific test and a positive response to an adequate treatment (e.g. a positive fungal culture and a positive response to antifungal treatment for cats with dermatophytosis, or a positive skin scrape and a favourable response to acaricide treatment for a mite infestation). Response to therapy was not required when fully effective treatments did not exist for a specific condition, for example in the case of tumours. The diagnosis of nonflea HD was based on the exclusion of all other resembling conditions, the presence of compatible clinical signs (one of the patterns described above) and a positive response to glucocorticoids, ciclosporine or type I antihistamines. A 6–8 week restriction diet followed by a 2 week (maximum) challenge with the previous diet (i.e. a dietary restriction–provocation test) was carried out whenever possible, but it was not a prerequisite for inclusion. Cats with signs of nonflea HD responding completely to the restriction phase and flaring upon challenges were given the diagnosis of food HD (i.e. food hypersensitivity-associated dermatitis). Pruritic cats with nonflea HD having no conclusive response to a restriction–provocation test were given the diagnosis of nonflea/nonfood HD, and they were suspected to have an HD associated with environmental allergens. Pruritic cats not subjected to a dietary restriction–provocation test, or those with inconclusive responses (for example cats with signs improving during the trial but not relapsing during the challenge, or outdoor cats not improving during the trial – because food HD cannot be excluded in these individuals) were assessed as having an undetermined HD and were excluded, and their data were not included in statistical analyses because a definitive diagnosis was a prerequisite for inclusion. Other specific tests (PCR, treatment with tricyclic antidepressant or selective serotonin reuptake inhibitors, skin histopathology) were carried out when required to rule out resembling diseases such as viral, psychogenic or neoplastic dermatoses, respectively. In prospective cases, pruritus was evaluated by the owners using a visual scale adapted from one designed for pruritic dogs (Figure 1).¹⁴

Statistical analyses

Based on their tentative diagnoses, cats were clustered in four groups for statistical analyses: those with flea HD, food HD, nonflea HD (including food HD and nonflea/nonfood HD) and finally those with other diseases (OD; being pruritic cats with a definitive diagnosis different from an HD). Continuous data were compared between groups using the Mann–Whitney *U*-test, whereas the proportions were compared using Fisher's exact test. Differences were considered statistically significant at the level of 5%. All analyses were carried out using GRAPHPAD INSTAT software (GraphPad, San Diego, CA, USA).

Results

Study population

Five hundred and eighty-eight cats presenting with pruritus were included in this study [correction added on 1st April 2011 after online publication: 'Five hundred and eighty-six cats' changed to 'Five hundred and eighty-eight cats']. Eighty-six cats had to be excluded because their diagnosis was unclear or two different diagnoses had been made. Altogether, data of 502 cats were available for review. The majority of initially included cats were of a domestic breed (European/American shorthaired/long-haired; $n = 405$). Most represented were the following breeds: Persian (36), Siamese (23), British shorthaired (17), ragdoll (15), Maine coon (14), Burmese (13), Norwegian forest cat (9) and Abyssinian (7). Bengali, oriental, Egyptian mau, Devon rex, Angora, Cornish rex, Balinese,

How itchy is your cat?

This scale is designed to measure the severity of itching in cats. Itching can include scratching, biting, licking, chewing, nibbling, rubbing and/or sudden run away. Read all the descriptions below **starting from the bottom**. Then use a marker pen to place a mark anywhere on the vertical line that runs down the left hand side to indicate the point at which you think your cat's level of itchiness lies.

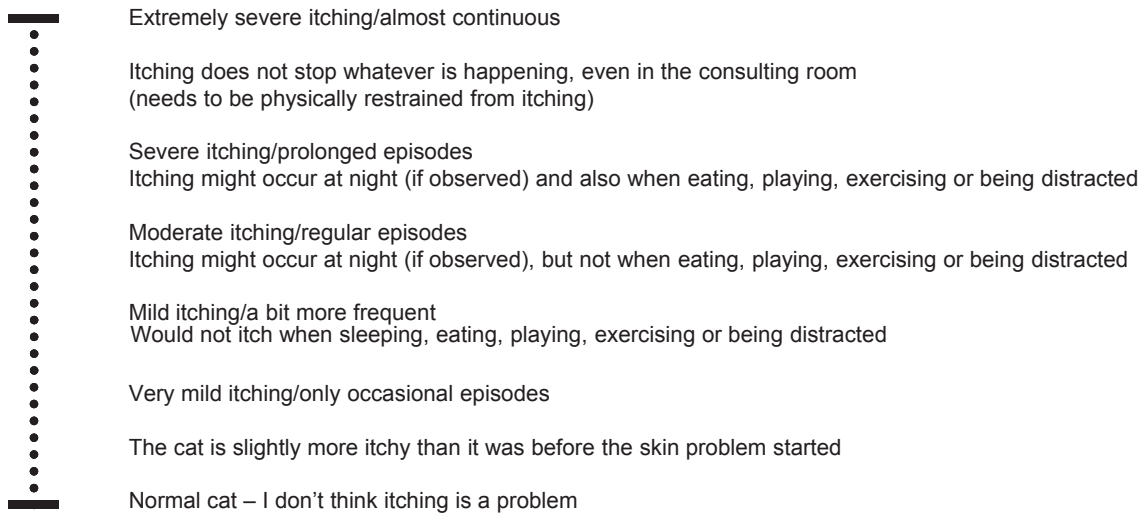


Figure 1. Pruritus scale.

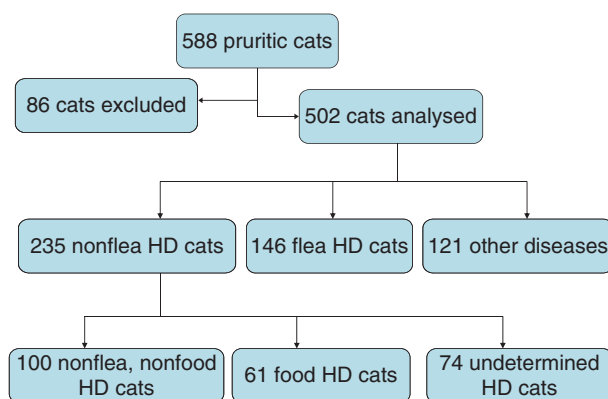


Figure 2. Assignment of cats into study groups.

Somali, sphinx, Chartreux and British blue were also represented but in low numbers. There were 225 male (45%) and 277 female cats (55%).

One hundred and forty-six cats were diagnosed with flea HD (29%), 61 with food HD (12%), 100 with nonflea/nonfood HD (20%), 74 with an undetermined HD (15%) and 121 (24%) with other diseases (Figure 2). These pruritic cats with other diseases were diagnosed as having one of 31 different conditions of the following categories: parasitic ($n = 35$; 29%), autoimmune (15; 12%), fungal (13; 11%), neoplastic (8; 7%), psychogenic (6; 5%), viral (5; 4%), isolated otitis externa (5; 4%) bacterial (4; 3%), and miscellaneous or idiopathic conditions (38; 31%). There were a total of 129 cats – some with more than one disease.

Clinical features of cats with nonflea HD

Results are presented in Tables 1–4 and Figure 3.

Forty-three of 161 cats with nonflea HD (27%) were purebred cats; all Abyssinian cats included in this study

belonged to this group. Males represented 41% of cats diagnosed with nonflea HD. The mean age of onset of pruritus was 3.4 years, and 82 cats with nonflea HD (51%) were younger than 3 years of age when they had their first pruritic episode.

Most cats with nonflea HD exhibited one of the following lesional patterns: self-induced symmetric alopecia (83; 52%), head and neck pruritus (95; 59%), eosinophilic diseases (41; 25%) or miliary dermatitis (30; 19%). Most cats (152 of 161; 94%) were affected with at least one of these patterns, while 74 (46%) presented with more than one. In the remaining nine cats (5%), erythema, nonsymmetrical alopecia and/or crusts were observed. Of cats evaluated prospectively, the mean pruritus score was 6.4 of 10, and 119 of 136 cats (88%) had a pruritus score of 5 or greater [correction added on 1st April 2011 after online publication: '119 of 161 cats (74%)' changed to '119 of 136 cats (88%)'].

Interestingly, two body areas were affected in more than half of the cats with nonflea HD: the head or face and the abdomen (Table 3 and Figure 3). Additionally, ears and neck were affected in more than one-third of cats included in this group. Conversely, paws, sternum or axilla and mouth were affected in <10% of these cats.

Sixty-seven cats with nonflea HD presented with non-dermatological signs (42%). Among these 67 cats, 22 (33%) exhibited digestive signs (e.g. diarrhoea, vomiting, soft stools or increased defecation), 24 (36%) had otitis externa, 13 (19%) had conjunctivitis and 10 (15%) had respiratory signs.

Comparisons between cats with nonflea HD and those with flea HD

Female and purebred cats were over-represented in the nonflea HD group compared with cats having flea HD ($P < 0.0001$ and $P = 0.003$, respectively; Table 1). In fact,

Table 1. Signalment and history data

	(1) Nonflea HD	(2) Nonflea HD/ nonfood HD	(3) Food HD	(4) Flea HD	(5) OD	(1) versus (4)	(1) versus (5)	(2) versus (3)
<i>n</i>	161	100	61	146	121			
Male cats (%)	66 (41)	42 (42)	24 (39)	83 (57)	48 (40)	<0.0001	n.s.	n.s.
Purebred cats (%)	43 (27)	22 (22)	21 (34)	22 (15)	35 (29)	0.003	n.s.	n.s.
Siamese	8 (5)	5	3	5	3	n.s.	n.s.	n.s.
Persian	11 (7)	4	7	7	12	n.s.	n.s.	n.s.
Abyssinian	5 (3)	3	2	0	0	n.s.	n.s.	n.s.
Maine coon	4 (2)	2	2	3	3	n.s.	n.s.	n.s.
Mean age at onset (years)	3.4	3	4	4.4	4.9	0.001	0.001	n.s.
Indoor:outdoor ratio*	76/64	46/42	30/22	49/73	53/53	0.02	n.s.	n.s.
Rural:urban ratio*	55/103	37/67	18/36	45/96	42/72	n.s.	n.s.	n.s.
Seasonality (%)	14 (9)	12 (12)	2 (3)	13 (9)	9 (7)	n.s.	n.s.	n.s.
Pruritus mean	6.4	6.4	6.4	5.7	4.9	0.001	0.0001	n.s.
Pruritus < 5 (%)	17 (13)	10 (11)	7 (14)	32 (24)	45 (45)	0.008	<0.0001	n.s.
Pruritus > 5 (%)	98 (72)	64 (73)	34 (69)	79 (57)	42 (42)	n.s.	<0.0001	n.s.
Pruritus = 5 (%)	22 (16)	14 (16)	8 (16)	26 (19)	13 (13)	n.s.	n.s.	n.s.

Means and proportions were analysed using Mann–Whitney *U*-test and Fisher's exact test, respectively.

HD, hypersensitivity dermatitis; n.s., not significant; OD, other disease.

*Cats living in both environments were not taken into account.

[Corrections to Table data added on 1st April 2011 after online publication: 'Rural:urban ratio*' row data were changed, as were data in the bottom 3 rows of '(1) Nonflea HD' column].

Table 2. Pattern and pattern associations

	(1) Nonflea HD	(2) Nonflea HD/ nonfood HD	(3) Food HD	(4) Flea HD	(5) OD	(1) versus (4)	(1) versus (5)	(2) versus (3)
<i>n</i>	161	100	61	146	121			
Miliary dermatitis (%)	30 (19)	18 (18)	12 (20)	51 (35)	11 (9)	0.001	0.02	n.s.
Eosinophilic granuloma complex (%)	41 (25)	26 (26)	15 (25)	20 (14)	3 (2)	0.01	<0.0001	n.s.
Erosions/ulcerations face and neck (%)	95 (59)	56 (56)	39 (64)	55 (38)	66 (55)	0.0002	n.s.	n.s.
Symmetrical alopecia (%)	83 (52)	57 (57)	26 (43)	57 (39)	22 (18)	0.02	<0.0001	n.s.
At least one of previous four presentations (%)	152 (94)	95 (95)	57 (94)	133 (91)	90 (74)	n.s.	<0.0001	n.s.
Multiple patterns (%)	74 (46)	46 (46)	28 (46)	41 (28)	9 (7)	0.007	<0.0001	n.s.

Proportions were analysed using Fisher's exact test.

[Correction to Table data added on 1st April 2011 after online publication: 'At least one of previous four presentations (%)' row data were changed under column '(3) Food HD'].

Table 3. Localizations

	(1) Nonflea HD	(2) Nonflea HD/ nonfood HD	(3) Food HD	(4) Flea HD	(5) OD	(1) versus (4)	(1) versus (5)	(2) versus (3)
<i>n</i>	161	100	61	146	121			
Head/face (%)	93 (58)	56 (56)	37 (61)	62 (42)	57 (47)	0.008	n.s.	n.s.
Ears (%)	54 (34)	32 (32)	22 (36)	31 (21)	58 (48)	0.02	0.02	n.s.
Chin (%)	28 (17)	17 (17)	11 (18)	21 (14)	15 (12)	n.s.	n.s.	n.s.
Lips (%)	23 (14)	15 (15)	8 (13)	8 (5)	7 (6)	0.01	0.05	n.s.
Oral/mouth (%)	11 (7)	2 (2)	9 (15)	6 (4)	3 (2)	n.s.	n.s.	n.s.
Neck (%)	66 (40)	36 (36)	30 (50)	52 (36)	27 (22)	n.s.	0.001	n.s.
Rump/tail (%)	24 (15)	18 (18)	6 (10)	78 (53)	10 (8)	<0.0001	n.s.	n.s.
Forelimbs (%)	42 (26)	34 (34)	8 (13)	30 (21)	18 (15)	n.s.	0.03	0.003
Hindlimbs (%)	51 (32)	40 (40)	11 (18)	31 (21)	14 (12)	0.04	<0.0001	0.005
Forepaws (%)	11 (7)	6 (6)	5 (8)	5 (4)	14 (12)	n.s.	n.s.	n.s.
Hindpaws (%)	9 (6)	1 (1)	8 (13)	6 (4)	9 (7)	n.s.	n.s.	0.002
Lateral thorax (%)	24 (15)	17 (17)	7 (11)	14 (10)	12 (10)	n.s.	n.s.	n.s.
Sternum/axilla (%)	17 (11)	10 (10)	7 (11)	12 (8)	9 (7)	n.s.	n.s.	n.s.
Flanks (%)	16 (10)	14 (14)	3 (5)	28 (20)	8 (7)	0.02	n.s.	n.s.
Abdomen (%)	85 (53)	59 (59)	26 (43)	73 (50)	27 (22)	n.s.	<0.0001	0.05
Perineum (%)	20 (12)	14 (14)	6 (10)	18 (12)	5 (4)	n.s.	0.02	n.s.
Dorsum (%)	30 (19)	23 (23)	7 (11)	61 (42)	18 (15)	<0.0001	n.s.	n.s.

Proportions were analysed using Fisher's exact test.

[Correction to Table data added on 1st April 2011 after online publication: 'Neck (%)' row data were changed under column '(5) OD'].

Table 4. Associated clinical signs

	(1) Nonflea HD	(2) Nonflea HD/ nonfood	(3) Food HD	(4) Flea HD	(5) OD	(1) versus (4)	(1) versus (5)	(2) versus (3)
<i>n</i>	161	100	61	146	121			
Nondermatological signs (%)	67 (42)	42 (42)	25 (41)	44 (30)	49 (40)	0.02	n.s.	n.s.
Digestive signs (%)	22 (14)	9 (9)	13 (21)	17 (12)	10 (8)	n.s.	n.s.	0.03
Respiratory signs (%)	10 (6)	6 (6)	4 (7)	5 (3)	5 (4)	n.s.	n.s.	n.s.
Otitis (%)	24 (15)	20 (20)	4 (7)	4 (3)	23 (19)	0.0002	n.s.	0.02
Conjunctivitis (%)	13 (8)	8 (8)	5 (8)	4 (3)	8 (7)	0.04	n.s.	n.s.

Proportions were analysed using Fisher's exact test.

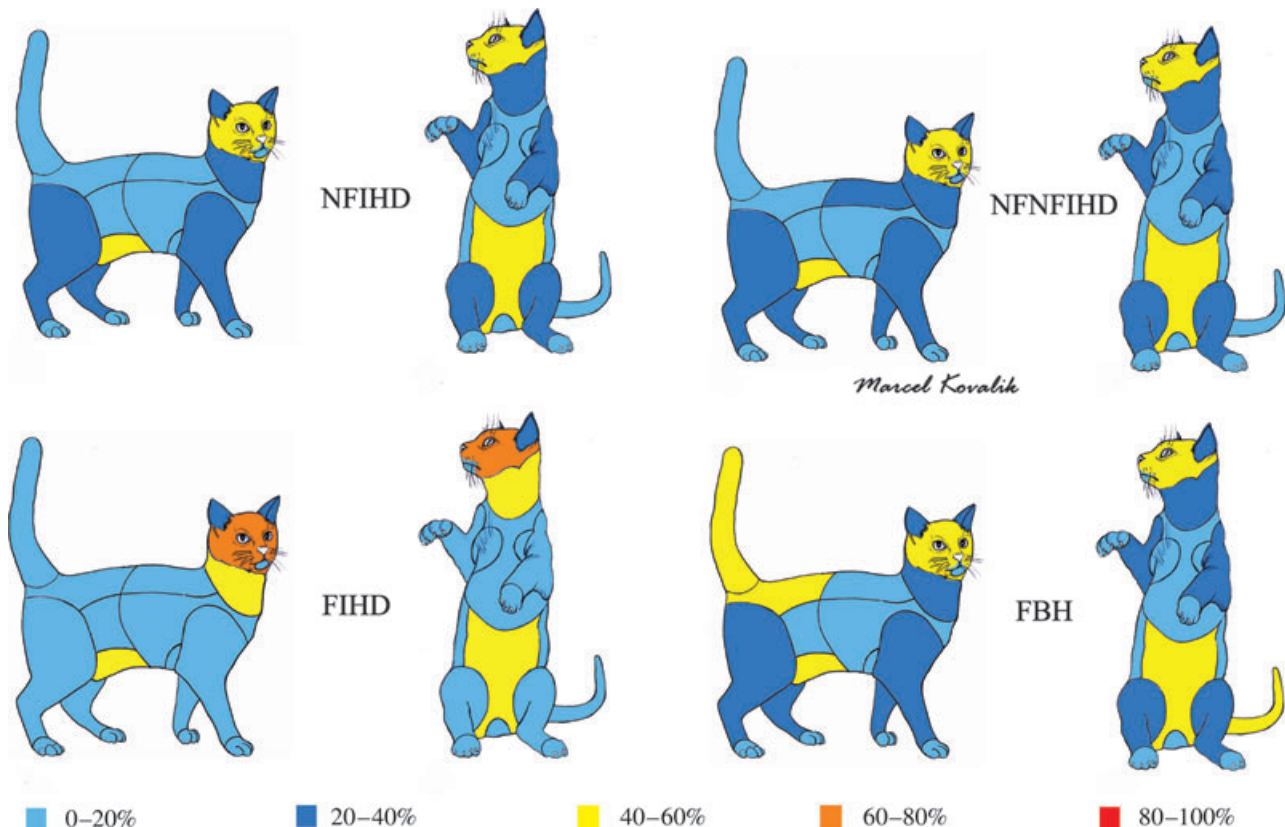


Figure 3. Silhouettes depicting the proportion of distribution of lesions in cats with nonflea HD, nonfood HD, food HD and flea HD. NFHD, non food induced hypersensitivity dermatitis; NFNFIHD, non flea, non food induced hypersensitivity dermatitis; FIHD, food induced hypersensitivity dermatitis; FBH, flea bite hypersensitivity.

when compared with the rest of the study population, males were over-represented in the flea HD group, while females dominated the nonflea HD group. Among pure-bred cats, Abyssinians were only present in the nonflea HD group. The mean age at onset was also lower in the nonflea HD group (3.4 years) when compared with the flea HD group (4.4 years; $P = 0.001$). The pruritus was also more intense in cats with nonflea HD (6.4 versus 5.7 grade; $P = 0.001$).

Cats from both groups presented with one of the four main lesional patterns, but the frequencies of each pattern varied significantly between groups (Table 2); cats with flea HD presented more frequently than cats with nonflea HD with miliary dermatitis (35 versus 19%; $P = 0.001$) and less commonly with eosinophilic diseases (14 versus 25%; $P = 0.01$), head and neck excoriations (38 versus 59%; $P = 0.0002$) and symmetrical alopecia (39 versus 52%; $P = 0.02$). Interestingly, cats with

nonflea HD (46%) presented more often with two or more lesional patterns compared with cats having flea HD (46 versus 28%; $P = 0.007$).

The distribution of skin lesions was also different between groups (Table 3). The head or face ($P = 0.008$), the ears ($P = 0.02$), the lips ($P = 0.01$) and the hindlimbs ($P = 0.04$) were more frequently affected in cats with nonflea HD, while those with flea HD presented more often with changes affecting the rump or tail ($P < 0.0001$), the flanks ($P = 0.02$) or the dorsum ($P < 0.0001$).

Comparisons between cats with food HD and those with nonflea/nonfood HD

There were few significant differences between cats of these two groups. The mean ages of pruritus onset were similar in both groups; 72 cats with nonflea/nonfood HD (72%) and 32 cats with food HD (52%) exhibited their first pruritus manifestation before 3 years of age ($P = 0.04$). In

contrast, 26% of cats with food HD and 12% of those with nonflea/nonfood HD were first affected after their sixth year ($P = 0.02$; Table 1). Cats with food HD presented more frequently with lesions affecting the head or face and neck (Table 3). On the contrary, those with nonflea/nonfood HD usually exhibited a more widespread distribution with abdomen and extremities significantly more commonly affected than in cats with food HD. Finally, cats with food HD presented significantly more often with digestive signs, while otitis externa was more frequently associated with the diagnosis of nonflea/nonfood HD (Table 4).

Comparisons between cats with nonflea HD and those with other diseases

Cats from the OD group were affected with very heterogeneous diagnoses, making the validity of some parameters of little relevance. Nevertheless, several clinical patterns were rarely seen in cats from this group (Table 2), for example symmetrical alopecia (22 cats; 18%), miliary dermatitis (11 cats; 9%) or eosinophilic diseases (3 cats; 2%). In these cats, lesions rarely affected the abdomen, neck and hindlimbs (Table 3). In contrast, cats from this group often presented with erosions and ulcerations of the face and neck (55%).

Discussion

The main objectives of the present study were to review parameters from a large, geographically diverse population of pruritic cats and to compare groups of cats with various diagnoses. Compared with previous reports, the inclusion of numerous subjects recruited by dermatologists from various countries was aimed at reducing the selection bias normally associated with small numbers or local studies. However, this advantage could also be regarded as a drawback, as multicentre studies are typically associated with an inherent variability. Moreover, the proposed inclusion criteria, which covered the exclusion of resembling diseases and also the response to therapy, were meant to avoid diagnoses solely based on clinical features as well as to follow the typical work-up of cats with pruritus. These were more stringent criteria than those used in the previous reports.

This study first confirmed that most cats with nonflea HD present with signs of one of the four major patterns commonly associated with feline HD: miliary dermatitis, head and neck pruritus, symmetrical self-induced alopecia or eosinophilic diseases, the latter including eosinophilic plaques, eosinophilic granulomas and indolent ulcers. We also confirmed that none of these clinical patterns was pathognomonic for nonflea HD because cats from other groups (e.g. those with either flea HD or OD) could also present with similar phenotypes. However, the association on the same cat of two or more of these patterns was more frequently encountered in cats with nonflea HD than in those with other diagnoses.

Our results established that purebred cats, especially Abyssinians, were more often affected with nonflea HD than crossbred cats. In the authors' interpretation of the data, this observation suggests that a genetic cause could

underlie, in some patients, the development of nonflea HD. Female cats were more often affected with nonflea HD, while male cats were most commonly seen in the flea HD group; these data could suggest the association of these conditions with some unique behavioural or hormonal differences, or merely the fact that male cats were found to be kept most often outdoors. This overrepresentation of females among cats with HD was recently reported in another study.¹⁵

Several body areas (e.g. the head, neck, abdomen and limbs) appeared clearly associated with nonflea HD. These three areas are also very commonly affected in dogs with AD.¹⁶ The main difference between the typical lesional distributions of canine AD and feline nonflea HD are that the paws are more frequently affected in dogs with AD, but in this study it was rare in cats.¹⁶

In this study, we excluded numerous cats from analysis because a dietary restriction–provocation test had not been carried out or completed. Interestingly, these cats with 'undetermined HD' were very likely to be affected with nonflea HD, as most parameters from this group of cats were identical to those from the nonflea HD group (data not shown).

As expected, cats with flea HD often presented lesions in the dorsal aspect of their body (rump, tail and dorsum), this distribution pattern mirroring that seen in dogs with flea allergy dermatitis. Interestingly, the head or face and the abdomen were also commonly affected in cats with this disease.

The comparison of clinical features between cats with nonflea/nonfood HD and those with food HD only revealed subtle differences. Although these differences were not statistically significant, the face and neck were more frequently affected in cats with food HD than in cats with nonflea/nonfood HD. Cats with the latter presented with a more widespread lesional pattern, which was more similar to that seen in canine AD. This study further established that the diagnosis of food HD cannot be made on clinical grounds alone, but that dietary restriction–provocation tests should be performed in cats with nonseasonal pruritus to evaluate the relevance of food involvement in the genesis of clinical signs.

Of importance, we observed that cats from the OD group also often presented with erosions or ulcerations from the head or neck. This observation suggests that this pattern is not pathognomonic for an HD – and especially a food HD – and that numerous conditions (parasitic, viral, fungal, autoimmune and neoplastic) must be ruled out before a diagnosis of HD can be made. In this study, 24% of cats presented with pruritus had a diagnosis other than one associated with HD, which underscores the need for clinicians to perform careful and complete diagnostic evaluations of pruritic cats.

In conclusion, this study confirms that there are no specific signs that can be regarded as pathognomonic for nonflea HD, and that the diagnosis must be based on the exclusion of resembling disease, especially flea HD. Nevertheless, as there were statistically significant differences in proportions or means between cats with nonflea HD and those with flea HD or OD, the association of several parameters could be helpful to improve the probability of diagnosis of a specific disease. The development

of a set of diagnostic criteria was beyond the scope of the present article, and these will be explored further in a forthcoming study.

Acknowledgements

The authors would like to thank Didier Carlotti, Paul Coward, Silvia Ruefenacht, Manolis Saridomichelakis, Nina Thom and Carla Dedola who also included some cases in this study.

References

1. Scott DW, Miller WH, Griffin CE. Skin immune system and allergic skin diseases. In: Muller and Kirk's Small Animal Dermatology, 6th edn. Philadelphia: W.B. Saunders Co., 2001: 543–666.
2. Foster AP, Roosje PJ. Update on feline immunoglobulin E (IgE) and diagnostic recommendations for atopy. In: August JR, ed. Consultation in Feline Internal Medicine, 4th edn. Philadelphia: W.B. Saunders, 2004: 229–38.
3. Reinero CR. Feline immunoglobulin E: historical perspective, diagnostics and clinical relevance. *Veterinary Immunology and Immunopathology* 2009; 132: 13–20.
4. Roosje PJ, Thepen T, Rutten VPMG *et al.* Feline atopic dermatitis. In: Thoday KL, Foil CS, Bond R, eds. *Advances in Veterinary Dermatology*, vol. 4. Oxford: Blackwell Sciences, 2002: 178–87.
5. Foster AP. Diagnosing and treating feline atopy. *Veterinary Medicine* 2002; 97: 226–40.
6. McCall CA, Steadmann KE, Bevier DE *et al.* Correlation of feline IgE, determined by Fc ϵ R1 α -based ELISA technology, and IDST to *Ctenocephalides felis* salivary antigens in a feline model of flea bite allergic dermatitis. *Clinical Advances: A supplement to Compendium of Continuing Education for the Practising Veterinarian* 1997; 3: 29–32.
7. Gilbert S, Halliwell REW. Feline immunoglobulin E: induction of antigen-specific antibody in normal cats and level in spontaneously allergic cats. *Veterinary Immunology and Immunopathology* 1998; 63: 235–52.
8. Halliwell REW, Gilbert SM, Lian TM. Induced and spontaneous IgE antibodies to *Demodex felis* in dogs and cats: evidence of functional heterogeneity of IgE. *Veterinary Dermatology* 1998; 9: 179–84.
9. Taglinger K, Helps CR, Day MJ *et al.* Measurement of serum immunoglobulin E (IgE) specific for house dust mite antigens in normal cats and cats with allergic skin disease. *Veterinary Immunology and Immunopathology* 2005; 105: 85–93.
10. Halliwell R. Revised nomenclature for veterinary allergy. *Veterinary Immunology and Immunopathology* 2006; 114: 207–8.
11. Johansson SG, Bieber T, Dahl R *et al.* Revised nomenclature for allergy for global use: report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. *Journal of Allergy and Clinical Immunology* 2004; 113: 832–6.
12. Prélard P, Guaguère E, Freiche V *et al.* The allergic cat. *Pratique Médicale et Chirurgicale de l'Animal de Compagnie* 1999; 34: 437–47.
13. Prost C. Les dermatoses allergiques du chat. *Pratique Médicale et Chirurgicale de l'Animal de Compagnie* 1993; 28: 151–64.
14. Hill PB, Lau P, Rybníček J. Development of an owner-assessed scale to measure the severity of pruritus in dogs. *Veterinary Dermatology* 2007; 18: 301–8.
15. Bexley J, Hogg JE, Hammerberg B *et al.* Levels of house dust mite-specific serum immunoglobulin E (IgE) in different cat populations using a monoclonal based anti-IgE enzyme-linked immunosorbent assay. *Veterinary Dermatology* 2009; 20: 562–8.
16. Favrot C, Steffan J, Seewald W *et al.* A prospective study on the clinical features of chronic canine atopic dermatitis and its diagnosis. *Veterinary Dermatology* 2010; 21: 23–31.

Résumé Les dermatoses par hypersensibilité (HD) sont souvent suspectées chez le chat. Les chats avec une HD sont rapportés comme pouvant présenter un ou plusieurs des patrons suivants : dermatite miliaire, dermatite éosinophilique, alopecie symétrique auto-induite ou excoriations de la tête et/ou du cou. Les rapports précédents sur les HD félines regroupaient un faible nombre d'animaux, issus d'espaces géographiques restreints et ne comparaient pas ces hypothèses aux autres causes de prurit. L'objectif de notre étude était d'analyser 72 paramètres incluant le signalement, la clinique et les caractéristiques de laboratoire et de traitement dans un large groupe de chats prurigineux issus de différentes zones géographiques. Sur les 502 cas, les diagnostics suivants ont été portés : hypersensibilité aux puces (29% des cas), hypersensibilité alimentaire (12%), autres maladies prurigineuses non-liées aux puces et non-liées à l'alimentation (24%). Les chats présentant des signes de HD mais n'ayant pas réalisés un régime d'éviction n'ont pas été inclus (15% des cas). La majorité des chats atteints de HD non-liée aux puces, ont montré des signes compatibles avec au moins un des quatre patrons lésionnels typiques, mais aucun de ces patrons ne s'est révélé pathognomonique d'un diagnostic spécifique. Les HD liées à l'alimentation et les HD non-liées aux puces et non-liées à l'alimentation se sont révélées cliniquement indifférenciables. Les jeunes adultes, les chats de race ou les femelles sont apparus prédisposés à l'HD non-liée aux puces et non-liée à l'alimentation. Plusieurs diagnostics se présentant avec des patrons lésionnels similaires, une recherche clinique approfondie est nécessaire pour l'établissement d'un diagnostic spécifique.

Resumen Las dermatitis causadas por hipersensibilidad (HD) se sospechan con frecuencia en gatos. Los gatos con HD se presentan con uno o mas de los siguientes patrones: dermatitis miliar, dermatitis eosinofílica, alopecia simétrica autoinducida o excoriaciones de la cabeza y/o cuello. Estudios previos acerca de HD en gatos han incluido un numero limitado de animales, tuvieron lugar en áreas geográficamente restringidas o no compararon estas condiciones con otras causas de prurito. El objetivo del presente estudio fue analizar 72 parámetros que cubrían datos del animal, características clínicas, laboratoriales y tratamiento de un número elevado de gatos con prurito de diferentes áreas geográficas. De los 502 gatos se obtuvieron los siguientes diagnósticos: HD debido a pulgas (29% de casos), HD alimentaria (12%), HD no asociada con pulgas ni alimento (20%) y otras enfermedades con prurito (24%). Los gatos con signos compatibles con HD pero que no completaron una prueba alimentaria no se analizaron en mas detalle (15% de casos). La mayoría de los gatos con HD no asociada a pulgas ni alimento presentaron signos compatibles con uno o mas de los cuatro patrones de lesión característicos, pero ninguno de esos patrones fue patognomónico de un diagnóstico específico. La HD alimentaria y la HD no asociada con pulgas ni alimentos

fueron clínicamente indistinguibles. Adultos jóvenes, gatos de pura raza y gatos hembra estaban predispuestos a HD no causada por pulgas ni alimentos. Ya que muchos diagnósticos se presentaron con similares patrones, se requiere una evaluación clínica completa para el establecimiento de un diagnóstico específico.

Zusammenfassung Bei Katzen werden oft Dermatitiden aufgrund von Überempfindlichkeiten (HD) vermutet. Katzen mit HD werden mit folgenden Präsentationsformen beschrieben: miliare Dermatitis, eosinophile Dermatitis, selbst-induzierte symmetrische Alopezie oder Exkorationen am Kopf und/oder Hals. Frühere Publikationen über feline HD beinhalteten eine kleine Anzahl von Tieren, wurden in sehr beschränkten geographischen Lokalisationen durchgeführt oder verglichen diese Erkrankungen nicht mit anderen Juckreizursachen. Es war das Ziel dieser Studie 72 Parameter, welche Nationale, klinische Merkmale, Labor- und Behandlungscharakteristika einer großen Gruppe juckender Katzen aus verschiedenen geographischen Gegenden abdecken, zu analysieren. Bei den 502 Katzen wurden die folgenden Diagnosen gestellt: Floh HD (29% der Fälle), Futter HD (12%), „weder Floh noch Futter HD“ (20%) und andere Erkrankungen, bei denen Juckreiz ein Symptom darstellte (24%). Katzen, die Symptome zeigten, die kompatibel mit einer HD waren, die aber eine Eliminationsdiät nicht abschlossen, wurden nicht weiter untersucht (15% der Fälle). Die meisten Katzen, die keine Floh-HD aufwiesen, zeigten Symptome, die kompatibel mit einem oder mehreren der vier typischen Veränderungsmuster waren, wobei aber keines dieser Muster pathognomon für eine spezielle Erkrankung war. Futter HD und „weder Floh noch Futter HD“ konnten klinisch nicht unterschieden werden. Junge adulte, reinrassige und weibliche Katzen schienen prädisponiert für „weder Floh noch Futter HD“. Da sich viele Diagnosen klinisch mit einem sehr ähnlichen Veränderungsmuster präsentierten, ist eine genaue klinische Aufarbeitung für die Erstellung einer spezifischen Diagnose nötig.

要約 過敏性皮膚炎 (HD) はしばしばネコで疑われる。HD のネコは 1 つ、またはそれ以上の以下のパターンを示していると報告されている：粟粒性皮膚炎、好酸球性皮膚炎、自己誘発性対称性脱毛、頭部/頸部表皮剥離。過去の報告では、ネコの HD は限られた地域での少数を対象としたものであり、または他の瘙痒の原因と比較していなかった。本研究の目的、様々な地域で痒みを示す猫の大規模な集団におけるシグナルメント、臨床所見、検査所見および治療法など 72 のパラメーターを分析することである。502 頭のネコで以下のように診断しが下された。：ノミ HD (29%)、食物 HD (12%)、非ノミ/非食物 HD (20%)、痒みを特徴とする他の疾患 (24%)。持続性の HD を示すが除去食試験を行っていないネコはそれ以上の分析を行わなかった (症例の 15%)。非ノミ HD のほとんどのネコで典型的病変パターンのうち 1 つ以上の症状と矛盾のない症状がみられたが、それらのいずれの症状も特定の診断を行うには十分でなかった。食事性 HD と非ノミ/非食事性 HD は臨床的に区別できないことが判明した。食事性 HD と非ノミ/非食事性 HD は若い成ネコ、純血種、雌ネコに好発すると思われる。複数の疾患が同じような病変パターンを示すため、徹底した臨床的な検査が特定の診断には必要とされる。

Acknowledgment

I would like to thank everybody who was involved in my work and gave me support, especially:

Prof. Dr. Claude Favrot, chief of the Dermatology Department, Vetsuisse Faculty, University of Zürich, Switzerland, who gave me the confidence for this work, for contacting dermatologists all over the world, for collecting cases, for acceptance of the reference and for the support and patience throughout the whole project

Dr. Sylvia Wilhelm, senior assistant of the Dermatology Department, Vetsuisse Faculty, University of Zürich, Switzerland, for the supervision of me and the project, for including cases and for all the support

Dr. Paula Grest, department chief of diagnostic (histology/cytology), Department of Veterinary Pathology, Vetsuisse Faculty, University of Zürich, Switzerland, for discussing histology slides

Dr. Steffi Köbrich, alternative resident at the Dermatology Department, Vetsuisse Faculty, University of Zürich, Switzerland, for the support and for including cases

Dr. Sveta Belova, alternative resident at the Dermatology Department, Vetsuisse Faculty, University of Zürich, Switzerland, for the support and for including cases

Dr. Sabrina Meury, assistant of the Dermatology Department, Vetsuisse Faculty, University of Zürich, Switzerland, for the support and for including cases

Dr. Nina Fischer, resident at the Dermatology Department, Vetsuisse Faculty, University of Zürich, Switzerland, for the support and for including cases

Dr. Claudia Nett, Dipl ECVD/ACVD, TSK Hünenberg, Switzerland, for the support, for giving me the possibility of collecting cases at her clinic and for including cases by herself

PD Dr. Petra Roosje, chief of the Dermatology Department, Vetsuisse Faculty, University of Bern, Switzerland, for the support, for giving me the possibility of collecting cases at university and for including cases by herself and her team

Heska AG, Fribourg, Switzerland, for the support and analysis of the serum allergens

Novartis Animal Health, Basel, Switzerland, for the support, for funding me and for the statistical analysis

Last but not least I like to thank my parents and my friends for giving me support and patience throughout the project.

Curriculum Vitae

First Name/Name	Stefan Hobi
Date of birth	21.09.1980
Place of birth	Chur GR
Nationality	Swiss
Place of origin	Walenstadt-Berschis SG
1986 - 1992	Primary School Bad Ragaz, Switzerland
1992 - 1996	High and Middle School Bad Ragaz, Switzerland
1996 - 2001	Cantonal School Sargans (higher education entrance qualification), type b, Switzerland
2002 - 2007	Veterinary Medicine Studies at Vetsuisse Faculty, University of Zurich, Switzerland
2007	Graduation from University of Zurich in Veterinary Medicine Studies
2008 - 2009	Doctoral thesis and assistant at the Division of Dermatology, Clinic for Small Animals, Vetsuisse Faculty, University of Zurich, Switzerland
2010 - 2011	Internship at Tierärztlichen Spezialistenklinik (TSK) Dr. Fretz, Huenenberg, Switzerland
2011 -	Dermatology-Residency at Ludwig-Maximilian`s University Munich, Germany